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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,618	02/06/2006	Martin Kintrup	30187/41217	1749

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MARSHALL, GERSTEIN & BORUN LLP
233 SOUTH WACKER DRIVE
6300 SEARS TOWER
CHICAGO, IL 60606-6357

EXAMINER	
GANGLE, BRIAN J	
ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,618	KINTRUP ET AL.	
	Examiner	Art Unit	
	Brian J. Gangle	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *4,14-18,20,24 and 25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5-13, 19, 21-23, and 26-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and remarks, filed on 2/4/2009, are acknowledged. Claims 3, 13, 21, and 26 are amended. Claims 31-35 are added. Claims 1-35 are pending. Claims 4, 14-18, 20, and 24-25 are withdrawn as being drawn to nonelected inventions. Claims 1-3, 5-13, 19, 21-23, and 26-35 are currently under examination.

Objections Withdrawn

The objection to the specification for the use of the trademark TWEEN is withdrawn in light of applicant's amendment thereto.

New Claim Objections

Claims 1, 10, 19, 26, 32, and 34 are objected to because of the following informalities: The genus name *Treponema* should be italicized. Appropriate correction is required.

Claim Rejections Withdrawn

The rejection of claim 13 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is withdrawn in light of applicant's amendment thereto.

The rejection of claim 21, under 35 U.S.C. 112, second paragraph, as lacking antecedent basis for the limitation "the cardiolipin:lecithin:cholesterol" in lines 1-2, is withdrawn in light of applicant's amendment thereto.

The rejection of claims 1-2, 5-6, 10-11, 19, and newly submitted claims 21 and 26 under 35 U.S.C. 103(a) as being unpatentable over West *et al.* (Sex. Transm. Inf., 78:282-285, Aug. 2002) in view of Egglestone *et al.* (Communicable Dis. Pub. Health, 3:15-162, 2000), is withdrawn in light of the declaration under 37 CFR 1.132, by Martin Kintrup, filed on 2/4/2009.

The rejection of claims 1-3, 5-12, 19, and newly submitted claims 21-23 and 26-30, under 35 U.S.C. 103(a) as being unpatentable over Zarakolu *et al.* (J. Clin. Microbiol., 40:3064-6065,

Aug. 2002) in view of Sambri *et al.* (Clin. Diag. Lab. Immunol., 8:534-539, 2001), is withdrawn in light of the declaration under 37 CFR 1.132, by Martin Kintrup, filed on 2/4/2009.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5-13, 19, 21-23, and 26-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary.

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. Thus, Applicant assumes a certain burden in establishing that inventions involving physiological activity are enabled. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The instant claims are drawn to carriers for diagnosis and/or follow up of a *Treponema* infection comprising at least one immobilized cardiolipin and at least one immobilized *Treponema*-specific antigen.

Guidance of the specification/The existence of working examples: The specification contains a general discussion of the detection of anti-*Treponema* antibodies using cardiolipin and the *Treponema* pallidum antigens with the molecular weights of 47, 44.5, 37, 17, and 15 kD. The specification states that is was unexpected that one could immobilize cardiolipin on a solid carrier such that their reactivity with the antibodies of the patient's material is maintained because application to the solid carrier represents a high risk of destroying the epitopes. The specification describes preparation of the antigens and the test strip, stating that the cardiolipin was prepared in an ethanolic solution and both types of antigens were immobilized onto a nitrocellulose carrier by passive adsorption by applying drops of antigen solution. The strips were then incubated in a buffer with 0.383% TWEEN 20. When used for testing, the strips are incubated with buffer containing 0.383% TWEEN 20.

State of the art: Assays are known in the art where separate immunoassays are used to detect antibodies against cardiolipin and various *Treponema* protein antigens. West *et al.* disclose two tests for the detection of syphilis, the RPR test and RST (see abstract). As evidenced by the RPR product information sheets from Omega Diagnostics (Omega Diagnostics Ltd., IMMUTREP RPR product sheet) and Becton, Dickinson, and Company (BD Macro-Vue RPR Card Tests), the RPR test is an agglutination test where VDRL antigen (cardiolipin, lecithin, and cholesterol) is immobilized on carbon particles (a carrier). The RST is a immunochromatographic strip test that contains the 47 kD *Treponema pallidum* antigen immobilized in a line on a test strip (carrier), as well as a control line (see page 282, column 1, paragraph 1 and page 282, column 2, paragraph 3). Zarakolu *et al.* disclose an immunochromatographic test strip where the 47 kD treponemal antigen has been immobilized in a thin line on nitrocellulose strips. The strips also contain a line of anti-human IgG to serve as a control (see page 3064, column 2, paragraph 2).

According to the declaration, under 37 CFR 1.132, by Martin Kintrup, detergents are used to reduce nonspecific binding in immunoassays in order to achieve the sensitivity and specificity required for diagnostic tests. According to the declaration, cardiolipin molecules are

released from test strips by the presence of detergents such as TWEEN 20. The declaration states that using a TWEEN 20 concentration of 0.05%, the cardiolipin could not be detected on the test strips of the instant invention. Applicant submits immunoblots to support this assertion and has previously submitted immunoblots to show that a concentration as low as 0.01% is required for the cardiolipin to stay immobilized on the strip. The declaration also states that others in the art used techniques for immobilizing cardiolipin that are incompatible with protein antigens or nitrocellulose test strips. Applicant refers to WO 91/101138 which teaches "elaborate" techniques to allow lipids to withstand treatment with detergents. The declaration asserts that these methods would disrupt protein epitopes and would not allow binding to nitrocellulose membranes. The declaration also refers to the methods taught by Pedersen *et al.* and states that Pedersen used ethanol which would disrupt protein antigens. Finally, the declaration asserts that applicant required extensive experimentation to discover that the lipid antigen, protein antigen, and buffer influence each other and the sensitivity and specificity of the claimed test system and that it was surprising that cardiolipin antigenicity could be maintained at a level required for a diagnostic test while maintaining sensitive and selective reactivity of *Treponema* protein antigens on the same carrier because low detergent concentrations resulted in high, unspecific background reactions of the protein antigens while higher detergent concentrations solubilized lipid antigens from the carrier.

Based on the assertions made in the declaration and the guidance in the specification, one of skill in the art would have been unable to make and use the claimed carriers for the utility disclosed. Applicant has asserted in previous arguments (supported by the declaration) that a special means of immobilizing the cardiolipin to the solid carrier is required to prevent the cardiolipin from being solubilized under conditions which are required for the protein antigens. However, the method disclosed in the specification to create the test strips used precisely the conditions applicant has asserted will not work. An ethanolic solution of cardiolipin was dripped onto a test strip. The strip was subsequently treated with a solution containing 0.383% TWEEN 20, which is far greater than the 0.05% solution applicant has shown to solubilize the cardiolipin and prevent the strip from working. Applicant's entire declaration is directed to the idea that the correct method of immobilizing the cardiolipin is required and the correct concentration of detergent is required to allow the strip to function. However, the results shown in the figures of

the specification and the direction given in the specification are at odds with what is taught in applicant's declaration. Therefore, there is no indication of how to properly make and use the instantly claimed carrier.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Gangle whose telephone number is (571)272-1181. The examiner can normally be reached on M-F 7-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Brian J Gangle/
Examiner, Art Unit 1645

/Robert B Mondesi/
Supervisory Patent Examiner, Art Unit 1645